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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/896,226	06/29/2001	Eric J. Benjamin	AM100155	9422

25291 7590 08/18/2005

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EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 08/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/896,226	BENJAMIN ET AL.	
	Examiner	Art Unit	
	Shaojia A. Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/10/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 10, 2005 has been entered.

This Office Action is in response to Applicant's request for continued examination (RCE) filed June 10, 2005, and amendment and response to the Final Office Action (mailed March 10, 2005), filed June 10, 2005 wherein claims 1-31 and 43-66 have been cancelled.

Currently, claims 32-42 are pending in this application and under examination on the merits.

The following is new ground(s) of rejection(s). Applicant's amendment filed on June 10, 2005, wherein all previously rejected claims are cancelled. Therefore, all rejections of record in the previous Office Action dated March 10, 2005 are withdrawn.

In particular the obviousness-type double patenting rejections over U.S. Patent No. 5,780,497 and 5,780,497 in view of Sawicka (Pharmazie 1991, vol.46 page 519-521) of record in the previous Office Action dated March 10, 2005 are withdrawn since

the particular compounds claimed in the patent 5,780,497 are not the instant compounds in the pending claims 32-42, nor are those claimed in the patent 5,880,137.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 32-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Raveendranath et al. (WO 9919293, PTO-1449 submitted September 18, 2001) in view of Sawicka (Pharmazie 1991, vol.46 page 519-521, PTO-1449 submitted September 28, 2001).

Raveendranath et al. disclose a pharmaceutical composition comprising the instant particular compound, 2-(4-Hydroxy-phenyl)-3-methyl-1-[4-(2- piperidin-1-yl-ethoxyl)- benzyl]]-1H-indol-5-ol (see its structure at the bottom of page 37 and Example **15** at page 40 and a pharmaceutically acceptable carrier or excipients to be administered to a mammal; the testing results for the composition comprising Example **15** at page 42, 44, 46, 47) are also disclosed. Raveendranath et al. also disclose that the effective amount of the compound to be administered for treating diseases therein is a dose of from about 0.1 mg/day to about 1,000 mg/day; preferably, administration will

be from about 50 mg/day to about 600 mg/day in a single dose or in two or more divided doses (see page 29 line 23-25).

In particular, Raveendranath et al. teach that:

"Oral formulations containing the active compounds of this invention may comprise any **conventionally** used oral forms. including tablets, capsules, buccal, forms, troches, lozenges and oral liquids, suspensions or solutions. Capsules may contain mixtures of the active compound(s) with inert fillers and/or diluents such as the pharmaceutically acceptable starches (e.g. corn, potato or tapioa starch), sugars, artificial sweetening agents, powdered celluloses, such as crystalline and microcrystalline celluloses, flours, gelatins, gums. etc. Useful tablet formulations may be made by conventional compression, wet granulation or dry granulation methods and utilize pharmaceutically acceptable diluents, blding agents, lubricants, disintegrants, suspending or stabilizing agents, including, but not limited to, magnesium stearate, stearic acid, talc, sodium lauryl sulfate, microcrystalline cellulose, carboxymethylcellulose calcium, polyvinylpyrrolidone, gelatin, alginic acid, acacia gum, , xanthan gum, sodium citrate, complex silicates, calcium carbonate, glycine, dextrin, sucrose, sorbitol, dicalcium phosphate, calcium sulfate, lactose, kaolin, mannitol, sodium chloride, talc, dry starches and powdered sugar. Oral formulations herein may be utilize standard delay or time release formulations to alter the absorption of the active compounds)." (emphases added, see page 30 lines 1-19).

Raveendranath et al. do not expressly disclose the specific range of amounts of a filler and disintergrant components, a wetting agent, a lubricant, and a glidant in a pharmaceutical composition herein. The prior art does not expressly disclose the pharmaceutical composition herein further comprising an antioxidant.

Sawicka teaches that adding an antioxidant to a pharmaceutical composition is well known in the art and the stability of a pharmaceutical formulation may be increase by antioxidant addition. See abstract and the entire article.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to determine the specific range of amounts of a filler and disintergrant components, a wetting agent, a lubricant, and a glidant in a pharmaceutical composition herein, and to further add an antioxidant to a pharmaceutical composition herein.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine the specific range of amounts of a filler and disintergrant components, a wetting agent, a lubricant, and a glidant in a pharmaceutical composition herein since it is known that a pharmaceutical composition comprising the instant compound and a pharmaceutical carrier or excipient system in a pharmaceutical formulation comprising a filler and disintergrant components, a wetting agent, a lubricant, and a glidant based on the prior art.

In particular, according to Raveendranath et al., the determination and the optimization of amounts of known exicipients such as a known filler, known disintergrant components, a known wetting agent, a known lubricant, and a known glidant in a pharmaceutical composition are considered **conventional** to an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Further, one having ordinary skill in the art at the time the invention was made would have been motivated to further add an antioxidant to a pharmaceutical composition herein since adding an antioxidant to a pharmaceutical composition is well known in the art.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Claims 32-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. (EP 802183, PTO-1449 submitted June 10, 2005) in view of Sawicka (Pharmazie 1991, vol.46 page 519-521, PTO-1449 submitted September 28, 2001).

Miller et al. disclose a pharmaceutical composition comprising the instant particular compound, 2-(4-Hydroxy-phenyl)-3-methyl-1-[4-(2- piperidin-1-yl-ethoxyl)-benzyl]-1H-indol-5-ol (see its structure Example No. **97**, at the bottom of page 8; page 37-38, page 41 line 55) or 1-[4-(2-Azepan-lyl-ethoxyl-benzyll-2-(4-hydroxy-phenyl)-3-methyl-1H-indol-5-ol (see its structure Example No. **98**; page 37-38; page 44 line 17-27) and a pharmaceutically acceptable carrier or excipients to be administered to a mammal. The testing results for the composition comprising Example **97** and **98** at page 64, 72, 74, 46, 47 are also disclosed. Miller et al. also disclose that the effective amount of the compound to be administered for treating diseases therein is a dose of from

about 0.1 mg/day to about 1,000 mg/day; preferably, administration will be from about 50 mg/day to about 600 mg/day in a single dose or in two or more divided doses (see page 13 line 16-18).

In particular, Miller et al. teach that:

"Oral formulations containing the active compounds of this invention may comprise any **conventionally** used oral forms. including tablets, capsules, buccal, forms, troches, lozenges and oral liquids, suspensions or solutions. Capsules may contain mixtures of the active compound(s) with inert fillers and/or diluents such as the pharmaceutically acceptable starches (e.g. corn, potato or tapioa starch), sugars, artificial sweetening agents, powdered celluloses, such as crystalline and microcrystalline celluloses, flours, gelatins, gums. etc. Useful tablet formulations may be made by conventional compression, wet granulation or dry granulation methods and utilize pharmaceutically acceptable diluents, blding agents, lubricants, disintegrants, suspending or stabilizing agents, including, but not limited to, magnesium stearate, stearic acid, talc, sodium lauryl sulfate, microcrystalline cellulose, carboxymethylcellulose calcium, polyvinylpyrrolidone, gelatin, alginic acid, acacia gum, , xanthan gum, sodium citrate, complex silicates, calcium carbonate, glycine, dextrin, sucrose, sorbitol, dicalcium phosphate, calcium sulfate, lactose, kaolin, mannitol, sodium chloride, talc, dry starches and powdered sugar. Oral formulations herein may be utilize standard delay or time release formulations to alter the absorption of the active compounds)." (emphases added, see page 13 lines 25-37).

Miller et al. do not expressly disclose the specific range of amounts of a filler and disintergrant components, a wetting agent, a lubricant, and a glidant in a pharmaceutical composition herein. The prior art does not expressly disclose the pharmaceutical composition herein further comprising an antioxidant.

Sawicka teaches that adding an antioxidant to a pharmaceutical composition is well known in the art and the stability of a pharmaceutical formulation may be increase by antioxidant addition. See abstract and the entire article.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to determine the specific range of amounts of a filler and disintergrant components, a wetting agent, a lubricant, and a glidant in a pharmaceutical composition herein, and to further add an antioxidant to a pharmaceutical composition herein.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine the specific range of amounts of a filler and disintergrant components, a wetting agent, a lubricant, and a glidant in a pharmaceutical composition herein since it is known that a pharmaceutical composition comprising the instant compound and a pharmaceutical carrier or excipient system in a pharmaceutical formulation comprising a filler and disintergrant components, a wetting agent, a lubricant, and a glidant based on the prior art.

In particular, according to Miller et al., the determination and the optimization of amounts of known exicipients such as a known filler, known disintergrant components, a known wetting agent, a known lubricant, and a known glidant in a pharmaceutical composition are considered **conventional** to an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Further, one having ordinary skill in the art at the time the invention was made would have been motivated to further add an antioxidant to a pharmaceutical composition herein since adding an antioxidant to a pharmaceutical composition is well known in the art.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 32-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,479,535.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to a pharmaceutical composition comprising the instant particular compound 1-[4-(2-Azepan-lyl-ethoxyl-benzyll-2-(4-hydroxy-phenyl)-3-methyl-1H-indol-5-ol and a pharmaceutically acceptable carrier or excipients to be administered to a mammal.

Note that the patent 6,479,535 also discloses that:
"Oral formulations containing the active compounds of Formula (I) and (II) may comprise any **conventionally** used oral forms. including tablets, capsules, buccal, forms, troches, lozenges and oral liquids, suspensions or solutions. Capsules may contain mixtures of the active compound(s) with inert fillers and/or diluents such as the pharmaceutically acceptable starches (e.g. corn, potato or tapioa starch), sugars, artificial sweetening agents, powdered celluloses, such as crystalline and microcrystalline celluloses, flours, gelatins, gums. etc. Useful tablet formulations may be made by conventional compression, wet granulation or dry granulation methods and utilize pharmaceutically acceptable diluents, blding agents, lubricants, disintegrants, suspending or stabilizing agents, including, but not limited to, magnesium stearate, stearic acid, talc, sodium lauryl sulfate, microcrystalline cellulose, carboxymethylcellulose calcium, polyvinylpyrrolidone, gelatin, alginic acid, acacia gum, , xanthan gum, sodium citrate, complex silicates, calcium carbonate, glycine, dextrin, sucrose, sorbitol, dicalcium phosphate, calcium sulfate, lactose, kaolin, mannitol, sodium chloride, talc, dry starches and powdered sugar. Oral formulations herein may be utilize standard delay or time release formulations to alter the absorption of the active compounds)." (emphases added, see col.22 lines 36-60).

As discussed in the 103 rejections above, the instant claims are deemed to be obvious claim 1 of U.S. Patent No. 6,479,535.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Anna Jiang, Ph.D.
Primary Examiner
Art Unit 1617
August 12, 2005